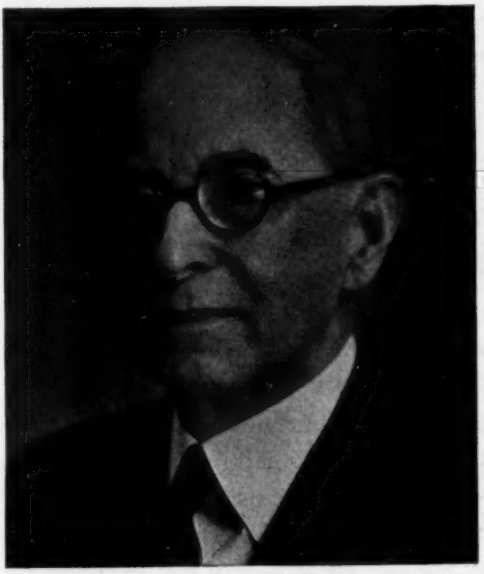
THE AMERICAN
JOURNAL OF PHARMACY

VOL. 108 MAY, 1936 No. 5

EDITORIAL

IN MEMORIAM



John Uri Lloyd

JOHN URI LLOYD is dead.

His spirit has at last entered into that realm, of whose reality his mind had never been uncertain. All of his useful, brimful life had been so ordered that the end, which inevitably comes, found here a soul, with all its elements, pure and wholly sublimable—totally worthy

of a condensing, reassembling space, there, where the Saints and the Gods foregather.

Sage and scientist, poet and prophet, dreamer and doer, master and mystic too, he had lived a life, abundant in service, durable in friendship, and divine in its serenity. The things that he knew, the principles that he taught, were tapped from those mysterious sources that yield their crystal fluids but to a favored few.

I like to remember him as last I saw him, talked with him, and found him, old indeed in years, yet supple and vigorous in mind—failing in sight—yet unrestrained in vision, and with a saintly mien that sent my comparing thoughts back to the word of God and to those grand old prophets of Israel.

It was on the occasion of the presentation to him of the first Procter award (1933). About him, then, was written the following:

"Eighty-five years rested none too lightly upon his shoulders, as in academic garb, he climbed the steps to receive from Dr. Wilmer Krusen, president of the Philadelphia College of Pharmacy and Science, a well-merited prize, the First Procter International Award.

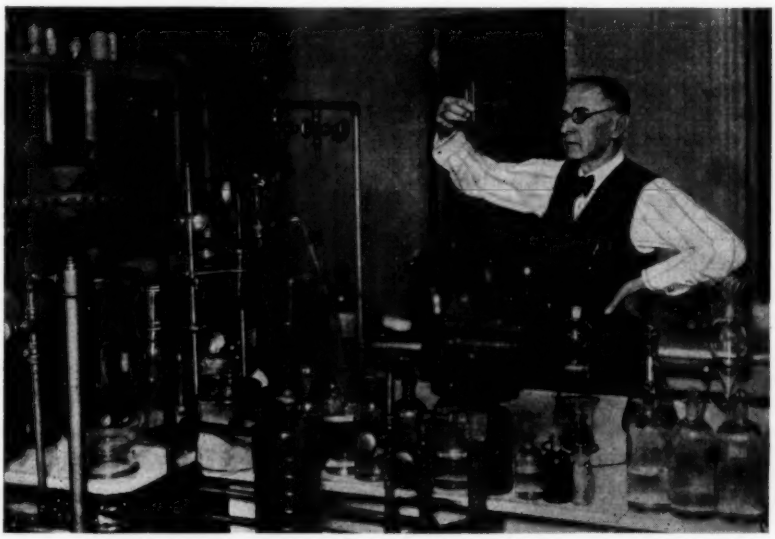
Yet when he stood up to speak he was at once alert, trigger-minded, rather quick moving and certainly belying his four-score and five.

His head, cocked a little to one side, his blue eyes sparkling from beneath his heavy glasses, his left hand raised, forefinger pointed heavenward—just as I had seen it pointed a quarter century ago before another audience—he said, 'Listen, young people,' and his audience young and old, knew at once that here was a man who had a right to their ears and a right to their hearts as well.

And he did not, as many old men do, censure the present day. It was a fine philosophy of life that he uttered—a definition of service—and that the truth makes all men free.

When he had finished—and he finished long before his audience wished him to—he withdrew and passed before a host of friends, missing none and intriguing all, with his modest kindly bearing.

Back to Cincinnati in the morning—and more than likely back to his test tubes and flasks."



In His Workshop.

Some years before Professor Martin H. Fischer, a recognized authority in the field of colloids, paid tribute to John Uri Lloyd in language so deftly arranged that it is a privilege and pleasure to quote him in full.

Said Dr. Fischer:

"I do not remember a time when, either alone or with a group of scientific friends, there was not in his first words a note of appreciation for their endeavors—a proof at once of his first-hand knowledge of the other man's life and the catholicity of his thought, for politicians, practical men, and theorists who put the modern builders of the atom to shame, all seek him out. Such greeting is followed by 'May I tell you a story?' And then some pearl, fitting well into the setting of the moment, is brought forth from his seventy-odd years of oyster life which even the great must pass through. In the pause which follows he speaks again: 'I have prepared an experiment which

I should like to show you.' In those who have had this experience several times, a warm rush of blood to the head is the emotional response which foretells that now some new decoration will be knocked off their scientific gargoyle. Do you hold the Guldberg-Waage law all sufficient; is the 'dew' on plants a settled question for you; do you think the tincture preparer of 1850 knew everything; is your view of solubility a crooked one because you know only water; is water itself just H_2O to you; is biology an undertaking confused in your mind; are you sure you know where the alkaloids come from; do you know why plants are green, or sometimes red, or maybe black; or why flowers are white and sometimes yellow? Answer carefully if your philosophy, your faith, or your religion are built up on the demonstrable in nature and not upon the interpolated texts of our scientific cook-book makers.

"You rise to go. You find your way out as you came in, but you are not as conscious as you were of the externals. You are more conscious of the internals. You have lost something—some of your scientific prejudices, some of your party adherences, some of your reverences for mere tradition. Also you have gained something—a more mobile state of mind, a larger tolerance, an increased generosity. And you are conscious that this is because for a little while you have been away from commissions, committees and boards, from diagrams, formulas, and fudge, and from canned efficiency, officialism, and Main Street, and for the same length of time have lived in the presence of the one thing that moves our universe, an individual and a man who is as good a picture in flesh and blood of what science stands for as may be found in a day's journey."

Such was the esteem in which this great man, co-worker in the colloid field, with Ostwald and other pioneers—a predicter of the day and the sway of the vitamin (he called them the "vital essentials" of the vegetable kingdom, long before their isolation)—such was the esteem in which Professor Lloyd was held by all his fellow workers in the vineyard of science.

John Uri Lloyd was born in New York State in 1849 of Welsh antecedents. He died April 10, 1936, at his daughter's home in California. His early education was obtained in private schools in various sections of the country. Strangely enough, he never received a college degree in course, but was awarded six different honorary degrees on six different occasions by six different colleges. Other honors, such as the American Pharmaceutical Association gold medals (1882, 1892,

1899), the Remington honor medal (1920) and the Procter Award (Philadelphia College of Pharmacy and Science, 1934) were bestowed upon him by appreciative scientific groups.

He was a teacher of note, an active member of numerous professional organizations and contributor to a large number of scientific publications, in addition to editing his own Lloyd Library Bulletin. His researches prompted him to delve into most of the many phases of pharmacy and chemistry, especially plant chemistry, alkaloids, glucosides, fluid-extracts and phytochemistry. The Lloyd Extractor, putting into practice the principle of continuous drug extraction, was the first of its kind to assume such large proportions. From his great and imposing array of test tubes and retorts, separators and stills, and every other conceivable type of apparatus that greeted the visitor to his laboratory, came many other noteworthy observations and conclusions.

But the thing for which John Uri Lloyd will be remembered by most people, probably, was his ability to observe human nature, study characters, watch how the "other half" lived, and then give his observations to the world in the form of technical tales, truly novel novels and folklore fantasies. His "Etidorpha," "Stringtown on the Pike," "Felix Moses the Beloved Jew," the last written in 1930 when he was 81 years old, and other books appealed equally to professional people, book lovers, romanticists and just plain readers, and they are destined to grace the front row of library shelves for centuries to come.

John Uri Lloyd was an altruist, and yet was practical enough to avoid waiting too long to practice his altruism, having set aside in recent years funds "for the purpose of encouraging the activities of Science promoting health."

He was a lovable, considerate, modest man, and there will be many fitting eulogies now that he has passed to his reward, even as there were many tributes paid to him while he was still with us.

God keep green his memory and give again his kind to a world so sadly needing such.

IVOR GRIFFITH.

ORIGINAL ARTICLES

NATIONAL AND INTERNATIONAL STANDARDS FOR MEDICINES*

By E. Fullerton Cook, P. D., Ph. M.†

UNIFORM standards for medicines is a recognized need for the medical world.

Many substances now used in the treatment of disease must be exactly controlled as to strength since they are often highly potent and require exact dosage if they are to produce the desired therapeutic effects.

E. Fullerton Cook

There is also the possibility of foreign substances finding their way into medicinal products, lessening their value or even adding an element of danger, and tests must be provided to rigidly guard against such a happening. This is not a new problem but its solution is being attacked with increased energy and with a degree of success which carries confidence to the physician and the patient.

degree of success which carries confidence to the physician and the patient.

In this program for the production of medical substances of dependable quality there is, in the main, a commendable coöperation between all of those who share the responsibilities.

This starts with the manufacturer who must maintain a scientific staff of reliable and skilled experts to select raw materials and to test these materials for conformity to the established standards of purity and strength. Another group of trained technicians must be responsible for the production and quality of the finished products. These medicines are widely varied. Among them will be found chemical salts; new synthetic compounds of a complex nature, such as arsphenamine; anesthetics, like ether, which are so important an

*One of the 1936 series of Popular Science Lectures of the Philadelphia College of Pharmacy and Science.

†Chairman of the U. S. P. Revision Committee and Director of the Pharmaceutical Laboratories at the Philadelphia College of Pharmacy and Science.

element in the safety of the surgical patient; or perhaps it is a biological product, illustrated by diphtheria antitoxin; or an ointment or a tablet, calling for skill and accuracy in manufacture.

These are but a few illustrations from among the hundreds of different medicines employed today.

After production and sale again the established standards apply and at this time with greater significance than before, since the tests are likely at any time to be made by the laboratories of enforcement officials with the possibility of substances being found unofficial and the manufacturer being charged with the adulteration of his products. This is all in the background of the production of modern medicines.

But you may be asking how this has developed. How were these medicines selected? Who discovered that some drugs are cathartics, that others cause a profuse perspiration, that another slows and strengthens the heart, while still others stimulate respiration or raise the blood pressure or perhaps relieve pain. We are particularly interested in knowing who determines the identity and quality of the medicines needed by modern physicians. What happened in past centuries is vaguely indicated by the records of the past.

In recent years this information about the value of new medicines has come through scientific researches in a modern laboratory, but the foundations were only slowly built up, through the centuries, by individuals who often worked alone, making crude observations and deductions and having few opportunities, and often no desire, to record the results for the benefit of others.

But fortunately there are remarkable exceptions and to these pioneers the world today acknowledges a debt of gratitude which is inestimable.

Back of all of this modern program is an interesting record. It is not necessary to review this in detail to remind you that the elaborate organization of today had its roots well grounded, first in tradition and then in proven history.

EARLY PHYSICIANS

The initial incentive of the pioneer healer is credited to an ennobling desire to relieve suffering. True, in every age the charlatan has exploited the sick for a pecuniary reward, yet the initial force, through all of history, seems to spring from those pioneers who truly labored to heal the sick and were a part of the religious orders of the time, theirs usually being a priestly service.

With the effort to help those who were ill, came some knowledge of the nature and causes of disease and with this there slowly evolved methods of treatment with all manner of strange medicines.

The early physician made slow progress; his knowledge was limited, the medicines were crude, he could not enforce treatments and he had poor opportunities to study effects. Yet it is surprising how many valuable substances had been discovered even when the oldest known records were revealed.

Of necessity there often entered into the treatment that which was associated with the mysterious or the occult, often with incantations and prayers—how natural that the influence of the diety should be evoked when the priest treated the sick.

EARLY MEDICINES

What medicines were used in the period of 4000 B. C., of Babylonian history, is not known, but tradition tells of the labors of the physician and of his associate who is supposed to have prepared the medicines.

Legend recounts the story of an Egyptian physician known by the name of Imhotep who lived about 3000 B. C., and he is reputed to have used many combinations of medicines.

A PAGE FROM THE "PAPYRUS EBERS"
From "The Evolution of Modern Medicine," Osler.
(Courtesy Yale University Press.)

That there is some justification for these unverified traditions of remote civilization is borne out by the discovery of an almost perfect Egyptian manuscript dated 1552 B. C., which consisted of a collection of medicinal formulas. This is called after the name of the discoverer, the Ebers Papyrus, and is evidently a record of the medicines known at the time when Moses lived and it must have represented the accumulated knowledge of the centuries. Here are recorded about 700 simple drugs representing the vegetable, animal and mineral kingdoms and while many were impossible and worthless it is remarkable that the list included substances which find a place even in the latest lists of present-day medicines. Among these were turpentine, castor oil, anise, henbane or hyoscyamus, poppy capsules, which were the forerunner of opium, aloes, myrrh, cassia, gentian, colchicum and squill.

Among the mineral substances were iron, lead, magnesia, nitre, vermilion, copper sulfate, sodium carbonate, and sodium chloride.

The use of precious stones, finely divided, was a form of medical treatment. These were ordered of various types and prices, depending upon the ability of the patient to pay. For the wealthy the emerald or lapis lazuli or the sapphire were directed, but for those less able to pay green porcelain or a similar appearing colored glass was acceptable.

This belief in the medical value of precious stones did not end with the Egyptian era for they are found in the pharmacopœias of Europe of the seventeenth and eighteenth centuries, showing how tradition and superstition can be continued for centuries.

Animal drugs were also present in abundance. It would seem as though the more offensive the more merit was anticipated. Certainly this early physician was willing to try every material at hand, hoping that he might discover that God-given remedy which he believed was provided as a cure for every disease. It would seem also as though they believed that special merit resided in any substance which had an offensive odor and so among the recorded animal drugs were lizards' blood, swine's teeth, putrid meat, stinking fat, moisture from pigs' ears, excreta from many sources, including flies and other substances even more revolting. Some of the formulas were very simple and evidently mild in action, as, for instance, one for headache calling for frankincense, cummin and an unidentified berry, all mixed with goose grease and applied externally.

On the other hand, some formulas were exceedingly complex; one for a poultice containing thirty-five ingredients with complicated directions for compounding. Evidently worm medicines were in demand for there were formulas for medicines to remove hookworms, tape worms, seat worms and intestinal worms.

Many forms of medicines had also been developed at this early period, including infusions, decoctions, fumigants, inhalations, gargles, injections, pills, powders, triturations, salves, plasters, confections and poultices. Here indeed was the forerunner of the modern pharmacopœia and a real attempt to establish some form of standards for the medicines then in use.

EARLY FORMULAS AND STANDARDS

Other medical papyri of this or even earlier Egyptian periods have since been discovered and some specialize in magic and sorcery which so frequently accompanied medical treatment.

While there is less known concerning the medicines of ancient China, probably because of less research into their literature, there is knowledge of a pharmacopœia-like compilation of Chinese formulas called the Great Herbal, which goes back beyond the Christian Era. It is made up of forty volumes and boasts of at least 1000 authors, including as the original authority the Chinese mythical god of medicine, Shen Nung. This work contains several thousands of prescriptions and many strange substances such as toad's eyelids for coryza. This particular drug might indicate a keenness of observation which is almost uncanny for modern investigations prove the presence of an adrenalin-like substance, secreted by a gland near the eye of a Chinese toad, and one of our modern treatments for coryza sprays the nostrils with solution of adrenalin.

Assyrian and Babylonian records also show about this same period a knowledge of medicines much the same as that of Egypt, evidencing the manner in which information is carried from country to country. Cannot one well imagine a wanderer upon the earth, carrying perhaps a secret recipe, in which some mysterious powder enters; a substance which may come from far off India or even China, by the routes of ancient commerce, and his selling it to physician priests far and wide for perhaps a fancy figure?

And so there is found, even in the earliest civilizations, a well-marked tendency toward established medical formulas, including

names, symbols and descriptions for hundreds of substances tried and recommended for the cure of the sick.

The great civilizations of Greece and Rome, covering more than 1500 years, were built upon the foundations laid by the still earlier races. They rose to heights of accomplishment in literature, architecture, philosophy, government and conquest not before dreamed of and they influenced the life and habits of all subsequent western peoples.

This is equally true in the field of medicine and the names of those who turned to the healing arts and recorded their observations and teachings, dominated medical practice in Europe for hundreds of years.

Tragically the later barbaric hordes or the fanatical religious groups who overran these countries in the middle ages destroyed countless manuscripts which could have added to the exact knowledge of the time, but enough was saved to preserve abundant evidence of the remarkable accomplishments of this productive period.

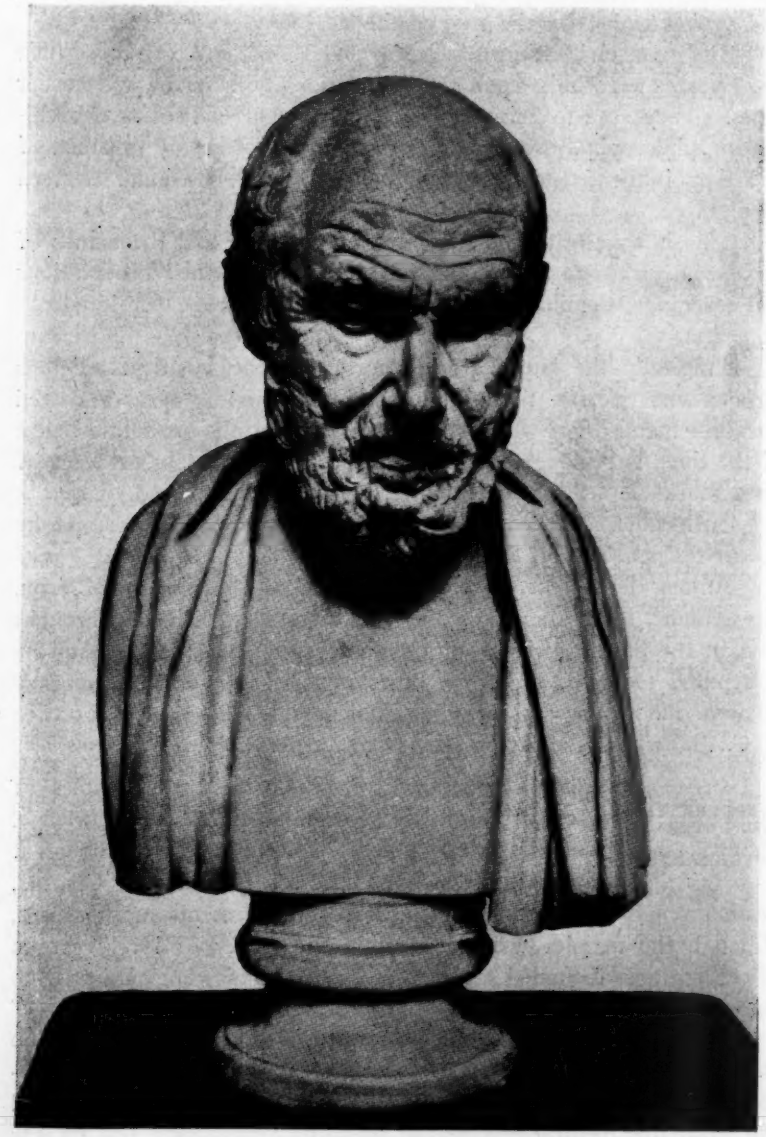
So blended are the earlier records that it is difficult to separate the mythological from the real.

Among the Greeks, Apollo was the God of Medicine, but Chiron, the Centaur, by mythological tale, was credited with having brought to man the first knowledge of the composition of medicines and he is reputed to have taught the other mystical characters what they knew of the healing art, including Aesculapius, who lived about 1250 B. C., and who is the patron saint of medicine.

HIPPOCRATES AND LATER GREEK PHYSICIANS

Prior to the time of Hippocrates, the temples of Aesculapius were the centers of medical knowledge, and the priests practiced the healing art although it apparently depended little upon medicines. Charms, incantations and prayers were the important elements in treatment, although the temples were situated in the center of lovely groves where springs abounded and where the patients were subjected to vigorous physical treatment.

Historically we owe to Hippocrates, a Greek physician born 460 B. C., the most exact knowledge of Greek medicine. He had apparently been steeped in the lore of tradition and mythology and had learned of the medical practices of previous civilizations, but his was that rare type who observes accurately and thinks clearly, and his writings sharply distinguished between the real and the supernatural



HIPPOCRATES
From "The Evolution of Modern Medicine," Osler.
(Courtesy Yale University Press.)

and recorded for future generations the knowledge which he had acquired in his long and active life.

In his writings he named about 400 medicinal substances and is said to have made his own preparations. While Hippocrates did not compile what might be called a pharmacopœia his books told of the uses of medicinal substances and how to combine them and since his teachings influenced medical practice for at least two thousand years, his place in the fixing of standards for medicines cannot be exaggerated.

During this period many new schools of medical thought arose and in most of them medicinal substances found a place.

In the post-Hippocratic period, reigned the famous Mithridates Eupator, King of Pontus. After his defeat by Pompey, the formula for his famous medicine was released. The *Confection Mithridates,* was improved upon by Damocrates, physician to Nero, and later by Andromachus, also a body physician of Nero. This became the most famous medicine of history. It was also known as *Confectio Damocrates* and as *Theriac* (as he added flesh of vipers—the name coming from *Tyrus,* a snake) and sixteen hundred years later the formula was included by Valerius Cordus in his dispensatory. At that time the traditional formulas contained about sixty ingredients.

Dioscorides was another Greek physician whose writings were long a dominant factor in European medicine and who was probably a contemporary of Claudius Galenus, commonly known as Galen. Galen was one of the most famous physicians of all history. He became a celebrated medical authority. He lived at the time of Marcus Aurelius and traveled widely, practicing his profession as he went. While born a Greek, he became a citizen of Rome. He was a voluminous writer on medical subjects as well as an experimenter in the preparation of medicines, many of which he made from vegetable drugs, and this class of products is still associated with his name, as "galenicals."

ROMAN ERA The first Roman to prepare a formulary was Scribonius Largus, physician to the Emperor Tiberius, about 45 B. C. This volume was called "Compositiones" and was more nearly of the type of the later pharmacopœias of the fifteenth, sixteenth and seventeenth centuries.

Besides the books which were being written, standard formulas were developed by individuals and passed on to future generations.

Reference has already been made to the Confectio Damocrates or *theriac*. Another formula, the theriac of Nicander, was written in verse on a stone in the temple of Æsculapius on the island of Cos, the birthplace of Hippocrates. Another *theriac* was that of Philon of Tarsus. This was written in verse that it might be more easily remembered. Its most rare ingredient was the "flesh of vipers" and this remained a part of the published formula 1500 years later. Another ingredient which might be misunderstood was written as "the red hair of a lad whose blood was shed on the fields of Mercury," but this was only the picturesque way to write "saffron." Other ingredients were opium, pyrethrum, euphorbium, pepper, henbane, spikenard made into a confection with honey. It was originally intended as an antidote to poison, but was widely used as a remedy for colic.

Then came the decline of Rome and its fall in the fifth century under the attack of the barbarians from the north who suppressed and destroyed these earlier civilizations. In the following centuries under the influence of Mohammed there began the period of Arabian supremacy. Egypt was overrun and in 642 Alexandria was captured and then the Arabs swept on through Spain and dominated most of the habitable world for 500 years.

Bagdad became an important center of learning and also Cordova at a later period.

ARABIAN PERIOD

Fortunately some manuscripts of Hippocrates and Galen had escaped the wholesale destruction of the libraries of Alexandria and were now translated into the Arabic together with other Greek scientific and philosophic writings. Fortunately the early intolerance of the Arabian Caliphs was abandoned and with the establishment of universities at both Bagdad and Cordova, teachers from the western world, Christians, Jews and Pagans, were encouraged to bring there the sciences in which they were interested. Medicine, pharmacy and chemistry were especially encouraged and under Caliph Haroun al-Raschid, about 780 A. D., hospitals and dispensaries and separate pharmacies were established in Bagdad.

An outstanding contribution to medical standards came about this time from Mesué Senior who was head of the Medical School of Bagdad during the reign of Haroun al-Raschid. His formulary

was translated into Latin as late as the fifteenth century and became the model for the first London pharmacopœia.

He was opposed to the violent purgatives of earlier medicine and is said to have introduced the mild laxatives senna, cassia fistula, tamarinds and jujube. His pupil, Johannitus, translated Galen's books into the Arabic, from which they were later translated into Latin.

The head of the hospital at Bagdad in 870 was a famous physician-pharmacist commonly known as Rhazes. He wrote voluminously on medicine and pharmacy and especially exposed many imposters.

Two hundred years later, another teacher, Mesué Junior, developed in Bagdad whose work entitled "Grabadin," which was an abbreviation of an Arabic word meaning compound medicines, was used as a pharmacists' manual for 500 years, going through hundreds of editions. It consisted of many formulas arranged in classes and many preparations of the earlier European pharmacopœias are traced back to this formulary.

Another eminent physician of the Arabian period was Avicenna, of the tenth century, and also Maimonides, the latter born at Cordova in 1135. Maimonides is most famous for his oath and prayer, setting forth an idealistic code of ethics for the physician and the pharmacist. It is almost as famous as the Hippocratic oath.

Contemporary with Haroun al-Raschid and the golden era of Bagdad, Charlemagne reigned. He encouraged the growing of herbs and the making of medicines by the monks. The herb gardens of the monasteries of Europe during the eighth and ninth centuries developed the vegetable materia medica and also a greatly increased knowledge of botany. The word "drug" also appeared about this time, meaning a "dry herb." With this development of the herbal garden there also appeared manuscripts dealing with drugs and their use in medicine, but they mostly dealt with charms and spells and contributed little to the knowledge of medicine.

During the ninth to the eleventh centuries, an opportunity was offered at Cordova for the establishment of a separate Jewish academy, and its influence rapidly spread through Europe where many Jewish physicians were welcomed and successfully practiced their profession.

One of the best known Italian Jews of this period was called Donnolo, and his "Antidotarium" contained descriptions and formulas for many drugs and preparations.

ELEVENTH TO FIFTEENTH CENTURIES

About the middle of the eleventh century there began a reawakening of interest in arts and sciences throughout all of Europe. The Norman Duke Robert captured Salerno in 1076 and encouraged the development of the university so that it became the leading educational center of middle Europe. During the next 200 years other universities were established—Paris, Bologna, Oxford, Cambridge, Padua and Naples—and in all of them medicine and pharmacy were taught.

The medical director of the Medical School at Salerno at the beginning of the twelfth century was Nicholas Praepositus. His "Antidotarium" became the standard for pharmaceutical formulas for centuries, and he introduced the apothecaries' system of weights and measures much as it is known today.

A notable advance came in 1224 when Frederic II of Sicily established a regulation requiring all physicians and compounders of medicine to be examined and licensed by the Medical School of Salerno. The pharmacists, or as they were then called, the "Confectionarii," were required to swear that they would prepare all medicines according to the instructions of the Antidotary of Nicholas Præpositus.

The drug dispensers were under strict inspection, and some preparations had to be made in the presence of inspectors. Any attempt to defraud subjected the offender to confiscation of his property and an inspector caught violating the law was subject to the death penalty.

During the next period, from the twelfth to the fourteenth centuries, many additional universities were established, but there was little original medical knowledge developed, although during this time frightful scourges swept through Europe, these including leprosy, ergotism, black death or plague, and later syphilis. It is estimated that 25 per cent. of the human race died from plague during this period.

This era is noted, however, pharmaceutically, for the establishment of regulations for pharmacists and the setting up of independent pharmacies and guilds governing their practice throughout much of the European world.

FIRST REAL PHARMACOPŒIA

In 1498 there was issued in Florence the first real pharmacopœia. This was compiled by a commission appointed for the purpose. It was made up mostly of the formulas of Galen, Mesué, Avicenna, Rhazes and Nicholas Præpositus. A second pharmacopœia appeared at Barcelona in 1535. It not only contained formulas, but also the rates at which drugs should be sold.

In the sixteenth century an "Antidotary" appeared in two volumes by John Jacob Wecker. In the second volume, of almost 900 pages, are printed thousands of formulas with the authorities for many and here are included most of the famous names in medicine for the past 1200 years. Here the Theriaca formula is attributed to Galen and it included sixty or more ingredients with a full page of directions of manufacture. Because Theriaca was believed to be a specific cure for the plague, it was largely in demand. Then came the compilation of formulas by Valerius Cordus, published by the order of the city of Nuremberg in 1546. This was more of a dispensatory type than a pharmacopœia although it was long looked upon as the first real pharmacopœia.

A similar compilation of formulas appeared in 1564, known as the Augsburg Pharmacopœia, and it also had much influence over later pharmacopœias.

LONDON PHARMACOPŒIA

But now came an outstanding event in pharmacopœia making—the appearance of the First London Pharmacopœia in 1618. It had been sponsored by the College of Physicians of London and special committees were appointed as early as 1589, but these committees had to be reorganized and it finally appeared almost thirty years later. It contained 1028 simple drugs and 932 preparations and was therefore quite an extensive work.

It did not depend wholly upon the older formulas handed down for centuries, but included many prescriptions attributed to contemporary authorities.

Here are found many familiar medicines of today, such as potassium bitartrate, sulfur, potassium nitrate, calomel, lead acetate, antimony oxide, aloe, calcium hydroxide, scamony and squill. There were also many revolting substances, especially among the animal drugs.

The appearance of the London Pharmacopœia stimulated the physicians of many other cities to issue pharmacopœias. In the list are Paris, Antwerp, Brussels, Edinburgh, Dublin and others under the names of countries, as Prussia, Saxony, Württemberg and Spain.

PHARMACOPŒIA OF THE UNITED STATES

It was chiefly the Pharmacopœias of London and Edinburgh, however, which inspired the first edition of our own United States Pharmacopœia.

To now turn to our own Pharmacopœia. We are accustomed, in this generation, to seeing strings of the letters of the alphabet everywhere we turn. This is so common that one wonders if there might not be a deficiency and a need for new symbols to express the many governmental or other activities constantly before the public. This custom was widely established during the World War (1914-1918), largely in the British Army, but has developed to a maximum in our own period of the "New Deal" (1933-1936). However, long before the alphabetic symbols of the World War or the New Deal were thrust upon us there have been known and used by physicians and pharmacists, three significant letters. They are "U. S. P." Today these are often seen by the public, and should have a meaning to the everyday man commensurate with the importance which they hold in relation to health. "U. S." naturally means the United States. "P." stands for a word long established but not often used by the public—the word "Pharmacopœia."

These letters, "U. S. P.," are frequently found upon labels of medicinal substances. They follow the title and indicate that the material in the package or bottle maintains the standards of strength and purity established by the Pharmacopœia of the United States. When a pharmacist orders medicinal substances for use in manufacture or in the filling of prescriptions, he usually writes "U. S. P." on the order. By this means he is assured of a high-grade product, uniform in quality and suitable and safe for medicinal use. If, when the layman enters a drug store and purchases certain of the commonly used and well-established home medicines, he insists upon having U. S. P. quality, there is the same protection for him as for those connected with the professions.

Uniformity in quality such as is now insured by U. S. P. standards was not always obtainable. The development of superior quality and consequent efficiency in medicinal substances represents many

years of cooperative effort on the part of physicians, pharmacists and the government. We are fortunate in having at our command this accumulated experience and an organization which establishes standards for medicine within the United States.

As has already been intimated, it was customary in the American colonies for physicians and apothecaries to employ the Pharmacopœias of Europe as the basis for the medicines. These were generally recognized as standardized. In the English colonies, the Pharmacopœias of London and of Edinburgh were employed, but soon after the establishment of the Republic the possibility of having a national pharmacopœia for the United States of America was recognized and given serious consideration. What is often spoken of as the "First American Pharmacopœia" was a small book or formulary compiled in 1778 by Dr. William Brown for use in the hospitals of the United States Army. The limited scope of this publication accounted for the failure to have its use extended into general medical practice. However, the physicians in general practice were ambitious to establish their own standards, and in 1787 a Committee of the College of Physicians in Philadelphia was appointed for this purpose. There is no record of any report from that committee.

In 1805 the Massachusetts Medical Society was responsible for the issuance of what became known as the Massachusetts Pharmacopœia, but this had only a local use and also was limited in its scope. In the main, the Massachusetts publication was based upon the Edinburgh Pharmacopœia.

The subject continued to be agitated and various medical centers prepared preliminary compilations embodying local or native plants, the Medical Society of South Carolina having done this as early as 1798.

The stimuli resulting from the appearance of the Pharmacopœia sanctioned by the Medical Society of Massachusetts was the nucleus for increased interest, and in 1815 the physicians and surgeons of New York had organized for the preparation of their own pharmacopœia. This appeared in 1816.

To one man is universally given the credit for the inspiration and the organizing ability which brought into existence the first edition of our national Pharmacopœia. That man was Dr. Lyman Spalding. He had long recognized the importance of this step and is known to have discussed the question with Dr. Barton, of Phila-

delphia, while visiting in that city in 1805. Dr. Barton was a professor of materia medica and editor of the Medical and Physical Journal. His botanical gardens had at that time acquired world fame and in these gardens he had particularly cultivated native medicinal plants. Dr. Spalding presented a well-formulated plan to his New York colleagues in January of 1817 and a committee was appointed to assist him in developing the program. This committee met and invited medical organizations in America and abroad to offer suggestions and to lend their support. In accordance with their plan, sectional conventions were called to consider the proposal to establish a pharmacopœia and each to send plans and outlines. Two of these sectional conventions met; one in Boston; and the second in Philadelphia. A third called as a "Southern Convention" failed to secure a quorum, but arranged for delegates to attend the Washington convention as did also those invited to form a "Western Convention." At the preliminary meetings in Boston and in Philadelphia very complete drafts for a proposed Pharmacopœia were prepared, the contents being largely based upon the then current pharmacopœias of London, Edinburgh and Dublin.

MEETING OF 1820 Following out the plan, representatives of these sectional conventions met in Washington, D. C., in the spring of 1820 and, after giving consideration to the various proposals, a committee was appointed to write and edit the new Pharmacopœia.

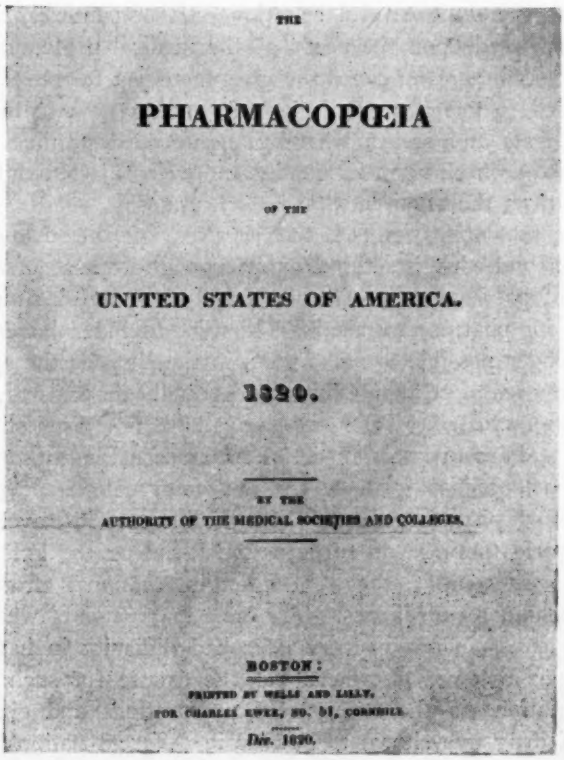
Dr. Spalding assumed the responsibility of chairmanship and editor, several meetings were held, and the new Pharmacopœia was issued the following December. This new book of standards received the general approval of the medical profession, and while there were some criticisms, the start had been made for national agreements upon the titles and quality of American medicines. Over 100 of the titles in the primary list of medicinal substances in this first Pharmacopœia have been carried forward into succeeding revisions, showing the careful character of the selections and the rather remarkable knowledge of medical substances at the beginning of the nineteenth century.

One important feature of this book was the number of formulas for chemical substances by which the apothecary could prepare or purify them for medicinal use. The list of vegetable drugs consisted mainly of titles and definitions with little effort to further standardize

the substances. There were, of course, formulas for making the popular preparations of the day.

In accordance with the traditions of the profession as exemplified by the pharmacopœias of that day, the text was printed on the left-hand page in Latin, with the translation in English on the right-hand page.

A feature of Dr. Spalding's original plan was the reassembling of the convention in each succeeding decennial year for the consideration of further revision of pharmacopœial standards. This program was carried through successfully from decade to decade, with a widening interest, and with the addition of pharmacists to the delegates at the 1850 convention. From 1820 to 1870 the general style of the Pharmacopœia remained the same except for the omis-


THE

PHARMACOPŒIA

OF THE

UNITED STATES OF AMERICA.

1820.

BY THE

AUTHORITY OF THE MEDICAL SOCIETIES AND COLLEGES.

BOSTON:

PRINTED BY WELLS AND LILLY,

FOR CHARLES EWER, NO. 51, CORNHILL.

Dec. 1820.

PHARMACOPŒIA OF 1820

sion of Latin, beginning in 1840, and the addition of new medicines as these were developed.

During this time the retail pharmacists made most of their preparations from selected raw material, often collecting their own vegetable drugs and there was no need for tests to prove that the official products conformed to the standard.

However, when the time came for the preparation of the Pharmacopœia of 1880, a new condition was rapidly developing. There had now grown up in the United States a number of chemical and pharmaceutical manufacturers who were selling ready made medicines to the retailer and this relatively new problem made it necessary to introduce tests and standards to check the products which were being sold. This began a new phase in pharmacopœial activity and largely altered the appearance and character of the book. There was the same careful selection of therapeutically important substances, based upon the needs of the medical profession, and in many instances there remained the manufacturing formulas for those who desired to use them, but the outstanding new feature was a series of tests and assays whereby the finished product could be subjected to a check upon its quality and even rejected if there was failure to meet the requirements.

With the expansion of the services of the manufacturing pharmacist and chemist, the Pharmacopœia dropped most of the methods of production for chemicals and also many manufacturing processes for pharmaceuticals. These were excluded because it was now no longer possible to make them in the shop of the apothecary with any degree of economy, but proportionally the tests for strength and quality increased. Tests and assays have now been still further expanded and are an essential part of the modern Pharmacopœia. Up to this time, practically all of the important nations of the world had their own pharmacopœias. With the increase in travel throughout the world there began to be agitated, during the latter part of the nineteenth century, the idea of an international effort for the standardization of medicines. The fact that patients who had secured medicines in one country later had difficulty in having their prescriptions renewed elsewhere was the excuse for such agitation. Great variations in the strength of preparations and even in the quality of drug was shown to be true in different national pharmacopœias, and considerable effort was made to develop what would

be known as an International Pharmacopœia. But this did not meet with general favor. This is natural, since national pride enters into the publication and also fundamental differences in the practices of various nations, so that strong opposition developed immediately.

The nations were not able or willing to agree upon one book of standards or formulas for medicines and the idea of an International Pharmacopœia was abandoned. However, there came a happy suggestion, originated apparently by the pharmacists of Brussels. This embodied the idea of setting up international agreements for specific items, these to be the more potent medicines. On the invitation of the Belgian Government, the various nations of the world were asked to send delegates to Brussels to consider the establishment of such standards and the first conference was convened in 1902.

By the plan announced, no nations would be influenced or persuaded against their wills to adopt in their forthcoming pharmacopœias the recommended strengths. On the other hand, there would be many advantages to each nation to have uniformity in the strength of the more potent remedies, and the plan met with wide favor—retaining as it did the inherent integrity of each national standard.

By this agreement, all preparations containing arsenic were made of uniform strength. Many other preparations which would be poisonous if taken in excessive dose were brought to a uniform degree of strength. For instance, a very important class of preparations—the tinctures—were made of 10 per cent. strength for all of those which were highly potent, including preparations of such drugs as digitalis, capsicum, opium, aconite, etc. Prior to this agreement, the strengths of potent tinctures varied from 5 to 50 per cent. and the new uniformity thus eliminated the danger of abnormal dosage or inferior therapeutic effects which might have resulted from the filling of a foreign prescription in a local apothecary shop. Tinctures of less active drugs were made 20 per cent.

THE FEDERAL FOODS AND DRUGS ACT

During the first eighty years of the existence of the Pharmacopœia of the United States, conformity to its standards was voluntary. It speaks well for the codes of ethics influencing the medical and pharmaceutical professions that this national standard was widely followed and the purpose of the Pharmacopœia thus carried out. However, for the maximum of efficiency, it was believed important to enact laws which would enforce uniformity in standards. Several

states had undertaken the passage and the enforcement of such laws and the question became a national issue. Under the aggressive leadership of Dr. Harvey W. Wiley, Chief of the Bureau of Chemistry of the Department of Agriculture, and with the enthusiastic support of many physicians and pharmacists, there was introduced into Congress and successfully passed what has become known as the Federal Food and Drugs Act. This law was actually passed in 1906. Under this legislation it is required that official medicinal substances shall maintain the strength and conform to the purity standards of the Pharmacopœia when sold or dispensed as medicines under the official names. There is a provision in the law which permits a modification of the official standards if this fact is clearly indicated upon the label. This is known as the "variation clause" and is intended to provide for justifiable modifications in official standards such as half-strength Tincture of Iodine. The basic principle underlying this law is represented by the principle that "The product must always be true to its label statement."

Following the establishment of this national drug law, which is operative only in interstate commerce and in the District of Columbia and the territories, most states passed similar laws to enforce the uniformity of standards for medicines within that state. Inspectors were appointed and specially trained chemists having established chemical laboratories were developed to enforce these laws and a high degree of uniformity in medicines was thus established. Recently Congress and the medical and drug world have been agitated by proposals that the Federal Food and Drugs Act be revised to be made more effective and also to include cosmetics within its scope. So far this law has not been passed, although several drafts have been given careful study and are now pending in Congress.

There is wide approval of such added legislation in the interest of public health and those who are affected have largely cooperated in trying to develop appropriate and enforceable laws.

KEEPING THE STANDARDS MODERN

If the descriptions and formulas established for medicines in 1820 were in force today they would be entirely inadequate. New medicinal products are constantly developed through the activities of medical research. Should these prove to be important therapeutic agents they properly find a place in the next Pharmacopœia and they call

for properly developed standards. Products which have long been official frequently need modified tests to control their degree of purity or to better determine their strength. Again, added tests are sometimes needed to check newly discovered foreign substances which appear in compounds, perhaps because of modifications in manufacturing procedure. In other words, there is a constant necessity for reviewing the standards of older compounds as well as establishing tests for those which are new.

In the last Pharmacopœial Convention, held in 1930, the delegates were mostly from the national and state associations and the colleges of both medicine and pharmacy. There were also representatives of the departments of the Government interested in health. These delegates developed the general policies governing the pharmacopœial revision and also elected the members of the Committee of Revision to revise the standards and a Board of Trustees to direct the business side of the organization. The Committee of Revision of the present Pharmacopœia numbers fifty-one with a large group of auxiliary members selected for their special ability or knowledge in specific scientific fields. The medical members of the committee are largely held responsible, in the initial stages of revision, for selecting the medicinal substances which are considered of sufficient importance to be officially recognized.

The other members of the committee are pharmacists, chemists, botanists, bacteriologists and others representing the many related sciences. These members assume the responsibility for fixing standards for those substances which are admitted. There is need for thorough knowledge of the botanical characteristics of drugs and the setting up of standards for these. Here the microscope is an important scientific instrument in determining the quality and identity of the drug. The plant structure or some specific micro-chemical test giving distinctive colors or crystals or reactions enter into the preparation of standards.

In a number of instances where there are specific crystalline principles of the alkaloidal type, as in cinchona which contains quinine and related alkaloids, as in nux vomica with its active principle strychnine, or in opium with morphine, codeine, etc., as the active agents, or in drugs of a similar character, tests are required by which these highly potent crystalline principles are extracted and their quan-

tity actually weighed or otherwise estimated. This method of procedure is known as a "proximate assay."

In other drugs the activities are represented by substances which cannot be extracted or weighed but the potency must be measured by their action on animals. For instance, the very important drug ergot has within it various alkaloidal substances which produce distinctive physiologic effects upon living tissue. One test which has been widely used depends upon the effect of one of these principles upon the comb of a rooster. The change is due to the contraction of the capillaries or small blood vessels in the comb causing it to become darker in color and the degree to which this is affected by known quantities of the drug, in comparison with a standard, is one means for determining its potency. Other biological tests, registering the actual effect of a drug upon an animal or one of its organs, must be used for the standardization of digitalis, aconite, pituitary, epinephrine and similar important and powerful drugs. In other cases, the absence of toxicity in a chemical such as arsphenamine is determined by injecting the substance into mice to assure freedom from dangerously toxic substances which might otherwise prove fatal to a patient. Other medicinal agents, chemical in nature, are standardized by many ingenious tests.

Frequently a reagent will bring about a distinctive color or a precipitation or cause some other reaction which indicates identity. Then the substance is usually tested for foreign substances or adulterants and again distinctive reactions result when standard reagents are added, and these indicate the absence or the presence of such foreign substances.

In the manufacturing of chemicals, there is always danger of introducing foreign materials. These may come from the apparatus used in manufacture or from the chemical substances entering the process or from other causes. So there are usually tests to exclude common adulterants. Another series of tests for almost all chemical substances deal with the identity of the product.

Chemicals are also frequently assayed by quantitative methods to determine their percentage of purity. Sometimes this is a simple chemical reaction such as the neutralizing of an acid with an appropriate amount of standard alkali, the indicator showing by color the point of neutrality and the calculation proving the degree of purity.

Other assays are much more complex but the objective is identical and the tests so applied that excessive amounts of foreign substances will be detected or the official quality of the material under investigation verified. Frequently the ingenuity of the chemist is tried to a high degree in maintaining accuracy and skill in carrying out these tests. Some assays are relatively simple, as for instance in the ointment of mercury in which the fatty vehicle is dissolved by a suitable solvent, leaving the metallic mercury which can be dried and weighed to determine the strength of the original ointment.

In recent years, a new series of tests have been developed dealing with the vitamin activity of cod liver oil. Only a few years ago it was demonstrated that there existed in this remarkable oil, at least two factors which were essential for health. A deficiency of either of these in humans, and especially in children, is often the cause of serious physical defects. The amount which is present in the oil under examination is determined by feeding it in measured amounts to rats which have been kept on a diet free from the vitamin under test, and with the animal consequently suffering the characteristic deficiency diseases. The amount necessary to restore the animal to health indicates the amount of the vitamin present. The results of such assays are based upon the average of a number of tests and can only be decided when they have been carried out over many weeks of experimentation.

That these official tests for identity, purity and strength may be effectively carried out, by both the producer of a product and the officials enforcing these standards, there is the necessity of thorough training and experience for the scientist carrying out the tests. This army of experts guarding the manufacturer and his products and those supporting the activities of officers of inspection in the Federal and State Governments represent a large group of scientific experts who are actively engaged in an important part of the health program.

The members of the Commission of Revision serve voluntarily as a contribution to the professions and to public welfare. This principle of voluntary service brings about an unusual degree of cooperation between the enforcement officials of the Government and the manufacturers of medicinal products and the experts in these fields associated with colleges and universities.

NATIONAL FORMULARY

While emphasis has been placed upon the Pharmacopœia as the book which fixes the standards for medicines within the United States, a second book called "The National Formulary" (abbreviated "N. F.") is also

recognized under the Food and Drug Acts and medicinal products sold under titles found in that book must conform to its standards unless a variation is clearly indicated on the label.

The U. S. P. and N. F. are not duplicates but each occupies a distinctive place in the medical field. The contents of the Pharmacopœia have always represented a selection of those therapeutically active agents which, in the judgment of the Revision Committee, were the most important of the decade in which the Pharmacopœia was issued. It also recognized such other substances as might be needed to standardize or from which to prepare these selected medicines.

The Pharmacopœia also restricted most of its therapeutic agents to "simples" rather than to combinations of these on the theory that a physician should write a prescription for each patient, combining the medicines, whether chemical or other substances, in the proportion and with the vehicle which he believed best suited to that particular patient.

The National Formulary, on the other hand, admitted and standardized other medicines which were sometimes used by physicians but which were not believed to be of sufficient importance or suitable for admission to the U. S. P. The N. F. also admitted some preparations of U. S. P. simples in the form of solutions or combinations, already prepared and suitable for the physician to prescribe without devising his own prescription. The N. F. also contained many older drugs and preparations for which there was some demand and a few new preparations which had not yet been sufficiently proven to receive pharmacopœial acceptance.

These two books, through their combined policies, are expected to include and standardize the medicines which are most frequently prescribed by physicians within the United States, but as they cannot give recognition to patented or trade-marked medicines, or those which are secret, there are many other medicinal products sold within the United States under private brands for which there is no official standard. However, under the Food and Drugs Acts, these unofficial products must conform to the claims made for them by the manufacturer and, while this is frequently evaded by the omission from the label of any specific statement as to strength or purity, the law operates effectively in some instances, especially when the product is a pill or tablet of an official substance and its strength must, of necessity, be given.

Another present day publication should also be mentioned, although it is not an official publication and its standards are not enforceable under the Food and Drugs Act. This is the *"New and Non-official Remedies"* of the American Medical Association.

This book lists mostly proprietary medicines but only those which comply with rigidly established rules which are enforced by the Council on Pharmacy and Chemistry of the American Medical Association. These rules require the elimination of all secrets as to identity and composition. They also regulate the type of advertising which may be used for non-professional publicity. All false or misleading claims must be avoided and the title must be acceptable to the Council and must not suggest its use in treating disease through self-medication.

The force of this publication resides in the desire of the owner of the product to occupy a favorable position before the physicians of the country and in this respect it has rendered an important service to the medical world through the maintaining of high standards of purity and conduct for many medicines which could not be controlled by the Food and Drugs Act under the U. S. P. or N. F.

Still another publication should be given recognition in the field of medical standards. This is the *"Official and Tentative Methods of Analysis"* of the Association of Official Agricultural Chemists. This is a compilation of standards and analytical methods published by the A. O. A. C. and accredited by the Secretary of Agriculture of the United States for use in the enforcement of food and drug standards in actions before the courts. The methods for testing were primarily for foods, but methods for testing unofficial drugs and preparations, especially tablets, have been added and thus establish an additional basis for the standardization of modern medicines.

THE INTERNATIONAL STANDARDS

An explanation of the observations of the so-called "Brussels Conference" has already been made. This first met in 1902 and a second session in 1925. The international character of this conference is indicated by the fact that in 1925 the representatives of thirty-two nations participated. As has been explained, the Brussels Conference agreed upon uniformity in standards for potent medicines, also upon the parts and varieties of the drugs to be used and established international titles. These recommendations were left to voluntary adoption by the participating nations in their forthcoming standards. Needless to say they have been widely accepted.

A new step in international standardization was brought about through the establishment of a Health Organization as a division of the League of Nations. This group have been particularly interested in the establishment of international standards for a class of medicines which are evaluated by testing on animals. They have undertaken the distribution of these throughout the world as a basis for uniformity in standards. In the biological division of the Organization, international standards have been set up for digitalis and posterior pituitary and also for the unit value for Vitamins A and D, for Vitamin B_1 and for Vitamin C and for the oestrus producing or ovarian hormone.

International standards have also been adopted for some of the biologicals including diphtheria antitoxin and tetanus antitoxin and also for arsphenamine. This international service is being utilized by the Pharmacopœias of the world in the establishment of a uniformity in potency for these very important medicines.

PROPOSED SECRETARYSHIP ON PHARMACOPŒIAS FOR THE LEAGUE OF NATIONS

The latest move for international agreement on pharmacopœial standards is an outgrowth of the last Brussel's Conference. This is the proposal that there shall be established as a division of the Health Organization of the League of Nations an office under the supervision of an international secretary for Pharmacopœias under whose direction there can be assembled for the benefit of all nations the scientific facts which have a bearing upon the standardization of medicinal substances. At the present time each National Pharmacopœial Commission is compelled to assemble this information independently and of necessity with a varying degree of completeness. If this were done for all the nations of the world through this international organization such a compilation of literature and experimental data could be issued to the participating nations in the language which they could use and thus another workable phase of international co-operation would be established, contributing to the general health of all nations.

THE LEAF OILS OF WASHINGTON CONIFERS: ABIES LASIOCARPA *[1]

By Charles Schwartz, Jr.

ABIES lasiocarpa (Hook.) Nutt, commonly known as "alpine fir", is a tree occurring in mountainous regions usually at altitudes above 5000 feet. Typical of trees growing at these elevations, it seldom reaches any great size. The height ordinarily varies from 3 to 90 feet, depending of course upon various factors, such as the altitude, exposure, and age of the tree.

The leaves and twigs, from which this oil was obtained, were collected in September, 1933, from trees growing in the Cascade Mountains, near the summit of Snoqualmie Pass. A total of 308 pounds of fresh material was gathered, which yielded on steam distillation 700 cc. of volatile oil, corresponding to 0.78 per cent. The oil was pale yellow, possessed a very aromatic, decidedly pinaceous odor, and dissolved readily in 95 per cent. alcohol.

The constants were determined and found to be as follows: $d_{\frac{20}{20}}$ 0.8828; n_D^{20} 1.4766; $[\alpha]_D^{23}$; —33.68; saponification number 47.360; acid number 0.365; ester number 46.995; per cent. of ester calculated as bornyl acetate 16.45; saponification number after acetylization 74.635; per cent of total alcohol, calculated as borneol 20.69; per cent of free alcohol, calculated as borneol 7.76.

Salicylic Acid: After removing the small amount of free acid by means of 5 per cent. sodium carbonate solution, repeated extractions were made with 5 per cent. sodium hydroxide solution in order to isolate phenolic compounds. The alkaline extract obtained was then shaken out with ether. Since the latter ethereal solution might contain carvacrol in addition to adhering oil, it was dried, evaporated spontaneously, and treated with ferric chloride solution. The color test for carvacrol was not obtained, however. The aqueous liquid was then acidified with dilute sulphuric acid and extracted as before with ether. This time, a crystalline residue consisting of white, fluffy needles remained, which represented approximately 0.5 per cent. of the original oil. The crystals, after purification with benzene, melted

*This paper is part of a thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy, and is the third of the series of three papers on the Leaf Oils of Washington Conifers.

1. Work done under the direction of Dr. Russell A. Cain, Instructor in Pharmacy, College of Pharmacy, University of Washington.

sharply at 158° C., and gave positive color reactions for salicylic acid. Their identity as salicylic acid was confirmed when admixture with the pure acid, also melting at 158° C., caused no depression of the melting point.

Fractionation: The residual oil was washed, dried, and then distilled several times up to 100° C. at 10 mm. pressure. The distillate obtained was again distilled to the same temperature at 10 mm. The combined residues and final distillate represented 30.44 and 64.00 per cent. by volume, respectively, of the original oil.

The lower boiling portion was fractionated and refractionated several times at atmospheric pressure up to 184° C. The following fractions were finally obtained:

Fraction	Temp. range	Volume	Per cent. by volume of Original Oil.	Rotation
I	150-160°C.	18.5 cc.	4.11	levo
II	160-163°C.	23.00	5.11	levo
III	163-169°C.	119.5	26.56	levo
IV	169-174°C.	75.00	16.67	levo
V	174-184°C	33.00	7.33	levo

Levo Alpha Pinene: Fraction I had a marked turpentine-like odor. It readily yielded a nitrosochloride melting at 115° C. after repeated precipitation from chloroformic solution by methyl alcohol. This derivative did not depress the melting point or pure alpha pinene nitrosochloride prepared from turpentine oil. A second portion of the fraction was oxidized with potassium permanganate as directed by Tiemann and Semmler (1). Pinonic acid was identified by its semicarbazone melting at 203° C., which further confirmed the presence of alpha pinene.

Levo Camphene: Fraction II was hydrated by means of acetic and sulphuric acids according to the method of Bertram and Walbaum (2). After saponifying the reaction product with alcoholic potassium hydroxide, the alcohol was removed by distillation. The resulting oil was washed well with water, extracted with petroleum ether, dried, and finally subjected to fractional distillation. Between 200 and 210° C., a borneol-like solid collected in the condenser. Upon treating the solid with phenyl isocyanate, a phenylurethane melting at 138° C. was obtained. The physical properties of the solid and

the melting point of the phenylurethane served to identify it as isoborneol, the hydration product of camphene.

Levo Beta Pinene: Fraction III represented a large share (26.56 per cent.) of the original oil. Oxidation by alkaline potassium permanganate solution according to the directions of Wallach (3) produced white, needle-shaped crystals, which melted at 126° C. after repeated recrystallization from benzene. No depression of melting point was noted when the product was mixed with a sample of pure nopinic acid. The preparation of this derivative identified the fraction as beta pinene.

Levo Beta Phellandrene: Fractions IV and V, together representing 24 per cent. of the original oil, proved to be identical in composition. Each yielded beta phellandrene nitrite, which melted at 102° C. after repeated precipitation from chloroformic solution with methyl alcohol.

Saponification and Fractionation: That part of the oil boiling above 100° C. at 10 mm. pressure was saponified by heating with alcoholic potassium hydroxide solution, after which the oil was separated, dried and fractionated under ordinary pressure. The following fractions were obtained:

Fraction	Temp. range	Volume	Per cent. by volume of original oil.
I	184-195°C.	10 cc.	2.22
II	195-230°C.	Solid	....
III	Residue	20	4.44

Borneol: Fraction I was a viscid liquid, which almost completely solidified when cooled by a salt-ice mixture. The solid material, separated by means of a suction filter, resembled camphor as to physical properties, as did also the second fraction. The solids from both fractions melted at 202° C. when recrystallized from ether, and formed phenylurethanes melting at 138° C. Admixture with pure borneol phenylurethane caused no depression of the melting point in either case, definitely identifying the fractions as borneol.

Fraction III: This fraction, consisting of the residue in the flask, was dark brown and viscous. By distilling it up to 250° C. at 85 mm. pressure, 9 cc. of yellowish, syrupy distillate was obtained. The latter liquid was dissolved in twice its volume of ether and the ethereal solution dried, after which dry hydrogen chloride gas was

passed through to saturation. The mixture was then allowed to stand for three days. No crystalline hydrochloride was obtained upon spontaneous evaporation of the solvent, suggesting the absence of sesquiterpenes.

Acids: Since salicylic acid had been previously identified in the phenolic extract, its presence in the free state was considered possible. The sodium carbonate washings of the original oil were therefore evaporated to dryness, and the residue tested for this acid. Negative results were obtained, however, indicating the salicylic acid to be present in the original oil probably in the form of an ester. Further examination of the very small amount of free acids was not made.

The aqueous potassium hydroxide extract from the saponification containing the combined acids was acidified with sulphuric acid and steam distilled. The distillate was turbid, had a little oily material floating on the surface, and possessed an odor which was very acrid and suggestive of rancidity. The mixture was neutralized with concentrated sodium carbonate solution and evaporated to dryness on a steam bath. The residue obtained responded to qualitative tests for acetic acid. In addition, small amounts of other volatile fatty acids were suspected because of the odor of the distillate.

A portion of the above residue was placed in acid aqueous solution and extracted with ether, since salicylic acid might also be present at this point. The small amount of residue remaining upon evaporation of the solvent, however, responded negatively to tests for this acid, from which it may be concluded that complete hydrolysis of the probable ester of salicylic acid had been accomplished by the 5 per cent. sodium hydroxide solution.

Summary: The leaves and twigs of Abies lasiocarpa yielded 0.78 per cent. of a volatile oil. The general constants of the oil were determined. The following constituents were found to be present in approximately the percentages stated: l-β-pinene, 26.56; l-β-phellandrene, 24.0; esters, chiefly bornyl acetate, 16.45; free borneol, 7.76; l-camphene, 5.11; high boiling residue, 4.44; l-α-pinene, 4.11; salicyclic acid, presumably as ester, 0.5 per cent.; also traces of free acids. Sesquiterpenes, if present, occurred in small amounts only.

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(1) Tiemann and Semler: *Ber.*, 28, 1344 (1895).
(2) Bertram and Walbaum: *Jour. prakt. Chem.*, 49, 1 (1894).
(3) Wallach: *Liebig's Annalen*, 356, 228 (1907).

CORRECTIONS IN THE UNITED STATES PHARMACOPŒIA, Eleventh Revision

Since the appearance of the new Pharmacopœia in December of 1935, the text has been subjected to intensive review and some corrections have been found necessary. Insofar as these cover typographical errors or accidental inaccuracies, authority has been given to publish the list of corrections in pharmaceutical and medical journals.

Purchasers of the new Pharmacopœia may also obtain a printed list of these corrections for insertion in their copies of the U. S. P. Send a 3-cent stamp, to cover postage, to the publishers of the Pharmacopœia, the Mack Printing Company, Easton, Pennsylvania.

Questions have also arisen concerning certain Pharmacopœial assays or tests and these are under investigation. In those cases where it becomes desirable to revise any of the printed monographs such changes will be announced by "Interim Revision" procedure.

Natural Water Versus Distilled Water in Drug Extraction, etc.

The new Pharmacopœia directs that distilled water shall be used in all formulas, but a further study of the difficulties involved has led the Committee to revise this requirement and permit the use of a *natural water* of good quality as an alternative to distilled water in the extraction of U. S. P. vegetable drugs and in the manufacture of Resin of Podophyllum and of Saponated Solution of Cresol. This is of the nature of an "interim revision" and a formal statement permitting the alternative use of natural water and establishing standards for it will be issued in the near future as an Interim Revision.

In addition to this revision of the distilled water requirement, other interim revision changes will soon be announced.

E. Fullerton Cook,
Chairman.

Page	Line	
lxx		Under Hydrastis and the sub-head Pulvis Hydrastidis *change* Hydrastis *to* Hydrastine.
lxxiv		*change* Theophyllina cum Sodii Acetas *to* Theophyllina cum Sodii Acetate.
19	4–6	*change to:* "Mix 0.5 Gm. of powdered Citric Acid with 5 cc. of sulfuric acid in a test tube that has been previously rinsed with sulfuric acid and maintain the temperature of the mixture at 90° C. for one hour: the color of the mixture is not darker than matching fluid K, described under the test for *carbonizable substances,* page 441."

Page	Line	
32	1–3	*change to:* "The potency of Aconite shall be such that 0.1 Gm. of it, when extracted and assayed as directed under *Tinctura Aconiti*, page 391, shall possess an activity equivalent to not less than 0.150 milligram of reference aconitine."
32		Fifth line from bottom of page: *change* 14.3 *to* 15.8.
78	1–4	*change to:* "The solution produced by dissolving 0.2 Gm. of Atropine Sulfate in 5 cc. of sulfuric acid has no more color than matching fluid A, described under the test for *carbonizable substances*, page 441, and the solution becomes only light yellow upon the addition of 0.2 cc. of nitric acid (*many other alkaloids*)."
96	33–46	*change to: Assay:* Weigh accurately in a glass-stoppered weighing tube about 0.4 Gm. of Calcium Bromide, dissolve it in 100 cc. of distilled water and add 1 cc. of hydrochloric acid. Heat the solution to boiling and add, with stirring, an excess of hot ammonium oxalate T. S., then make slightly alkaline with ammonia T. S. Heat the mixture on the water bath for two hours, filter through hardened filter paper and wash thoroughly with warm distilled water, puncture the filter paper, wash the precipitate into a beaker by means of a stream of hot distilled water, followed by 30 cc. of dilute sulfuric acid (1 in 3), heat the solution, if necessary, to 60° C. and titrate with tenth-normal potassium permanganate. Each cc. of tenth-normal potassium permanganate is equivalent to 0.009996 Gm. of $CaBr_2$.
97	43	*change* 0.05004 Gm. *to* 0.005004 Gm.
103	18	*change to:* "The specific rotation $[\alpha]_D$ of Natural Camphor, determined at 25° C., in a solution containing 10 Gm. of Camphor in sufficient alcohol to make 100 cc. and using a 200-mm. tube, is between + 41° and + 42°, page 459." Omit all reference to the specific rotation of Synthetic Camphor.
118	12	*change* 0.5 Gm. *to* 0.2 Gm.
125		Third line from bottom of page: *change* 0.5 Gm. *to* 0.01 Gm.
126	10	*change* 433.25 *to* 424.24.
127	32	*change* "0 45" *to* 0.45.
135	21–22	Add between the lines: Note—In preparing aqueous solutions of Dextrose it is permissible to use a dextrose which does not conform to the official requirements for water of hydration, provided the product meets all other official tests for purity and also provided suitable allowance is made for the difference in water content.
139	17	*change* 0.5 Gm. *to* 0.1 Gm.
150	12	*change* 0.3 Gm. *to* 0.03 Gm.
150	12	*change* 5 grains *to* ½ grain.
180	11–14	*change to:* Vigorously shake 5 cc. of Glycerin with 5 cc. of sulfuric acid in a glass-stoppered 25-cc. cylinder for one minute and allow the liquid to stand for one hour; it does not become darker than 10 cc. of matching fluid H, described under the test for *carbonizable substances*, page 441.
195		Fourth line from bottom of page: *change* 62 *to* 63.
195		Fifth line from bottom of page: *change* 61 *to* 60.
196	29–30	*change* "continue the heating" *to* "maintain the crucibles and mass at dull redness".
208	33	Add the synonym "Viosterol in Oil".
208	44	*delete:* "Unsaponifiable matter: not more than 2 per cent., page 446."

Page	Line	
231		Fourth line from bottom of page, *delete:* "natural".
231		Fifth line from bottom of page, *change* 42° and 44° C. *to* 41° and 43° C.
235		Fourth line from bottom of page, *change* 0.2 Gm. *to* 0.12 Gm.
278	21	*insert* before "Add": Place 100 cc. of distilled water in a 300-cc. Erlenmeyer flask, add 5 cc. of Paraldehyde, and shake the mixture gently until solution is complete.
289		Sixth line from bottom, *change* 0.5 Gm. *to* 0.1 Gm.
290		Twelfth line from bottom, *change* 0.5 Gm. *to* 0.1 Gm.
313	6	*change* 0.5 Gm. *to* 0.2 Gm.
313		Last line at bottom of page, *change* 0.5 Gm. *to* 0.2 Gm.
315	27	*change* 0.5 Gm. *to* 0.2 Gm.
316	14	*change* 0.5 Gm. *to* 0.2 Gm.
317	17	*change* 0.5 Gm. *to* 0.2 Gm.
318	22	*change* 0.5 Gm. *to* 0.2 Gm.
319	8	*insert* after "444": using about 1 Gm. of the Rosin accurately weighed.
321	5	*delete* "or" and insert after "species": (excepting *Rheum rhaponticum*) or of.
322	22	*change* 0.5 Gm. *to* 0.2 Gm.
324		line 10 from bottom of page, *change* 0.5 Gm. *to* 0.1 Gm.
353	30	*change* 25 cc. *to* 5 cc.
353	39	*change* 25 cc. *to* 5 cc.
362		Ninth line from bottom of page, *change* 0.5 Gm. *to* 0.1 Gm.
363	30	*change* 0.5 Gm. *to* 0.2 Gm.
368	31	*change* 7.243 *to* 7.281.
377		*insert* between the third and fourth line from bottom of page: "Alcohol content—From 1 to 2 per cent. by volume of C_2H_5OH."
378	27	*change* 7.5 to 8.5 *to* 8.5 to 11.
383	5	*change* 0.5 Gm. *to* 0.2 Gm.
384	20	*change* 0.5 Gm. *to* 0.2 Gm.
384	33	*change* 70 *to* 75.
384	34	*change* 80 *to* 85.
391	25–32	*change the directions to:* "Prepare a tincture by Process P, as modified for assayed tinctures, page 390, using a mixture of 3 volumes of alcohol and 1 volume of distilled water as the menstruum. Macerate the drug during twenty-four hours and then percolate it at a moderate rate. Immediately add sufficient hydrochloric acid to this percolate to produce a pH of 3 ± 0.2, page 576. Assay a portion of the percolate and adjust the volume of the remaining liquid by dilution with the above menstruum, including sufficient hydrochloric acid to produce a pH of 3 ± 0.2, page 576, so that the finished Tincture will conform to the above biological standard.
399		*insert* between the tenth and eleventh lines from the bottom of page: *Alcohol content*—From 58 to 64 per cent., by volume, of C_2H_5OH.
488	28	*change* 0.1631 Gm. *to* 0.1814 Gm.
572	25	*change* 0.02041 *to* 0.2041.
592	14	*change* 433.25 *to* 424.24.

CORRECTIONS IN NATIONAL FORMULARY VI

To be Made in Books No. 100,001 to No. 125,000

Issued by the National Formulary Committee with the approval of the Council of the American Pharmaceutical Association

Page	Line	
7	36	*change* One liter equals 1000.27 cc. *to* One liter equals 1000.027 cc.
33	22–26	*change to:* Ampuls of Dextrose contain a sterile solution of 50 Gm. of dextrose in a sufficient quantity of ampul water to make 100 cc., unless another concentration of the solution is stated on the label, and yield an amount of anhydrous dextrose, $C_6H_{12}O_6$, corresponding to not less than 86 per cent and not more than 96 per cent of the labeled amount of dextrose.
35	16–18	*change to:* solution is stated on the label, and yield an amount of anhydrous emetine hydrochloride, $C_{29}H_{40}O_4N_2.2\,HCl$, corresponding to not less than 84 per cent and not more than 92 per cent of the labeled amount of emetine hydrochloride.
35	39	*change* 0.006794 Gm. *to* 0.005533 Gm.
35	40	*change* $C_{29}H_{40}O_4N_2.2\,HCl.7\,H_2O$ *to* $C_{29}H_{40}O_4N_2.2\,HCl$.
41	6	*change* contained *to* contain.
45	27	*change* 0.005846 Gm. *to* 0.005845 Gm.
50	39–41	*change to:* Place 10 cc. of Water in a clean test tube and add 2 drops of methyl red pH indicator: no orange color develops, indicating a pH of not less than 5.8. Another 10 cc. portion of Water does not show a pink color.
52	10–14	*change to:* Macerate a weighed amount of the recently cut and partially dried dormant twigs of *Hamamelis virginiana* for about 24 hours in about twice their weight of water; then distil until not more than 850 cc. of distillate is obtained for each 1000 Gm. of the twigs taken; add 150 cc. of alcohol to each 850 cc. of distillate; mix thoroughly.
52	31	*change* 13 to 15 *to* 14 to 15.
53	33–37	*change to:* Place 10 cc. of Redistilled Water in a clean test tube and add 2 drops of methyl red pH indicator: no orange color develops, indicating a pH of not less than 5.8. Another 10 cc. portion of Redistilled Water does not show a blue color on the addition of 5 drops of bromthymol blue pH indicator, indicating a pH of not more than 7.0.
66	47	*change* 3.6724 Gm. *to* 3.7473 Gm.
68	26	*change* 1 cc. *to* 4 cc.
77	21	*change* didymium *to* neodymium, praseodymium.
89	45	*omit:* "Lutein"; transfer *or* to between "Extract" and "Copora Lutea."
112	21	*change* 22 to 24 *to* 23 to 26.
117	3	*change* 21 to 24 *to* 24 to 28.
122	13	*change* 1 cc. *to* 0.1 cc.
138	4	*omit:* 1 Gm. of the Extract represents 2 Gm. of aloe.
159	8	*change* 9.27 Gm. *to* 0.27 Gm.
162	3	*change* 57 to 63 *to* 52 to 57.
164	5	*change* 0.1 Gm. *to* 0.1 cc.

Page	Line	
164	13	*change* in each 100 cc., 3.75 U. S. P. *to* in each 0.1 cc., 3.0 U. S. P.
180	31	*change* 12 to 18 *to* 17 to 21.
187	3	*change* GEL. EPHED. *to* GEL. EPHED. SULF.
205	34	*change to:* Average dose: Metric, 1 Gm.—Apothecaries, 15 grains.
210	35	*change* 12 mm. *to* 10 mm.
244	25	*change* 8 Gm. *to* 6 Gm.
250	25	*change* Compositae *to* Composita.
317	38	*change* the walls *to* the cell walls.
353	14-a	*add:* DISTILLED WATER, a sufficient quantity.
372	39	*change* 10 cc. *to* 100 cc.
393	36-a	*add:* Dogs, 0.2 cc. per Kg. of body weight.
397	26	*change* 57 to 63 *to* 63 to 69.
397	27	*change to* : Average dose: Metric, 0.5 cc.—Apothecaries, 8 minims.
424	3	*omit:* Analgesic Balm.
434	3	*change* contain *to* each contains.
439	38	*change* Potassium Hydroxide *to* Sodium Hydroxide.
475	20	*omit:* (*Paris Green*).
494	11	*change* March 1 *to* June 1.

INDEX

Page	Column	Line	
515	2nd	33	*change* 473 *to* 474.
515	2nd	44	*change* 476 *to* 475.
535	2nd	27	*change* 313 *to* 131.
536	2nd	25	*change* Compositae *to* Composita.
537	2nd	2	*change* Mercurous Chloride, Iodide *to* Mercurous Iodide.
540	1st	24	*change* 475 *to* 479.
541	1st	12	*change* 434 *to* 435.
542	2nd	2	*change* Potassium Acetate, Hydroxide, *to* Potassium Hydroxide.
543	2nd	53	*omit:* Red, Phenol, Test Solution .....482.
544	1st	40	*change* Rocella *to* Roccella.
545	2nd	38	*change* 208 *to* 308.
545	2nd	39	*change* 340 *to* 240.

A list of these corrections, printed on one side of the sheet, is available, without cost, and is so arranged that the sheets can be inserted in the front of the N. F. VI, or that each correction can be cut out and pasted over the wording it is to replace.

Requests for the list of Corrections in the N. F. VI may be sent to Mack Printing Company, Easton, Penna., or to the American Pharmaceutical Association, 2215 Constitution Avenue, Washington, D. C., and *must be accompanied by a self-addressed envelope to insure delivery.*

SCIENTIFIC AND TECHNICAL ABSTRACTS

Compiled by Linwood F. Tice, M. Sc.

Permanent Pigmentation of the Skin Following the Application of Iron Salts. E. F. Traub and J. S. Tennen. *J. A. M. A. 106,* 1711 (1936). The use of iron salts in the treatment of ivy poisoning dates back to 1873. Many workers have recommended ferric chloride both for prophylaxis and the treatment of rhus poisoning, in fact some authors have suggested that it be the first choice in the chemotherapy of rhus dermatitis.

Ordinarily the use of iron salts in such cases is not followed by any undesirable sequelæ. The authors, however, call attention to two cases of permanent deep seated pigmentation which were produced by the treatment of rhus dermatitis by the external application of a solution of ferric chloride. By means of a punch biopsy instrument a small piece of tissue was removed from a pigmented area in one case and the nature of the pigmentation investigated. A large number of chromatophores were found about the blood vessels and between the collogen fibers of the upper corium.

Methods of removing the pigmentation were tried, e. g., ultraviolet radiations to produce peeling of the skin, without results. The authors feel that the use of iron salts applied as a lotion, compress or wet dressing should be discouraged in all vesicular, bullous, and exudative dermatoses.

An Inorganic Liquid Mixture for Temperature Baths in the Range 100° to 250° C. B. E. Christensen and A. E. King. *J. Ind. Eng. Chem. Anal. Ed. 8,* 194 (1936). The limitations of the substances commonly employed for temperature baths between 100° to 300° C. are quite well known. In the search for a suitable material for a temperature bath the following requirements were desired: (1) temperature range 125°-250° C.; (2) relatively high heat capacity; (3) no fuming at the temperature of operation; (4) transparency after long usage; (5) material easy to remove from glassware, and (6) no fire hazard. The organic substances commonly employed do not meet the five latter requirements; metal baths such as fusible alloys are objectionable due to their low heat capacities and high specific gravity; sulfuric acid not only must be used in the hood, but it is somewhat dangerous when handled hot.

Mixtures of ortho and metaphosphoric acids were investigated to learn if a satisfactory combination could be found which would provide an inorganic bath meeting the necessary specifications. A combination of 4 parts by weight of 85% orthophosphoric acid with 1 part of metaphosphoric was found to be quite satisfactory. Before mixing the acids each is slowly heated to 260° C. and kept there until the rapid evolution of steam ceases. The mixture is quite satisfactory as a temperature bath substance. It is mobile at room temperature, does not evolve H_2O vapor until a temperature exceeding 250° C. is reached, does not fume under 340° C. and, furthermore, it possesses a very small temperature gradient, as rising temperature causes expansion which results in the circulation of the liquid.

Carob Gum. W. A. Knight and M. M. Dowsett. *Pharm J. 136,* 35 (1936). Carob gum (Ceratoniæ gummi) is obtained from the seeds of the locust bean tree, *Ceratonia Siliqua,* a plant having a long history of usefulness and mentioned by Theophrastus (4th century B. C.).

Only recently has it been commercially possible to separate mechanically the gum containing endosperm from the other undesirable parts of the seed. This powdered endosperm constitutes the commercial product carob gum which upon analysis gave the following results:

Galactan	29.18
Mannan	58.42
Pentosans	2.75
Proteins	5.29
Nitrogen	0.83
Cellular tissue	3.64
Mineral matter	0.82

An enzyme, ceratoniase, is also present. The purified gum forms a solution at least equal in viscosity to that of tragacanth which it has already replaced in many products.

Several pharmaceutical products have been prepared with carob gum with very good results. A mucilage may be made by mixing 0.15 gm. of benzoic acid, 1.0 gm. of carob gum, 3.0 cc. of glycerin, adding 80 cc. of water and heating for 30 minutes, not only to aid in the formation of a good mucilage but to destroy the enzyme, cera-

toniase, which would otherwise cause loss of viscosity by hydrolysis. As an emulsifying agent carob gum was found somewhat superior to tragacanth. Several other formulas employing carob gum are presented.

Different Methods of Preparing Colloidal Sulfur. H. Schmidt-Hebbel and I. S. Pavez. *Pharm. Zentralhalle 77,* 265 (1936). The methods of producing colloids fall into two general classes: (1) *Condensation Methods* wherein molecularly dissolved material is caused to condense into a colloidally dispersed state, and (2) *Dispersion Methods* in which large particles are by mechanical, physical or chemical means caused to break down into the smaller colloid particles.

In most cases the condensation method of preparation is employed for preparing sulfur hydrosols. The method of change of solvent is quite common and it consists in preparing a molecular solution of the substance in a solvent and then pouring this solution into another solvent in which the substance is insoluble. For example a saturated solution of sulfur in hot alcohol is prepared by dissolving 0.5 gm. of sulfur in 100 cc. of boiling alcohol and then filtering. 5 cc. of this clear solution is then poured into a large volume of water with vigorous stirring to obtain a uniform dispersion. In this way a yellow dilute hydrosol of sulfur is obtained. The best condensation methods depend on oxidation reactions. Sodium thiosulfate is decomposed by sulfuric acid or hydrogen sulfide is oxidized by sulfur dioxide. In the former case the formation of thiosulfuric acid is followed by its immediate decomposition in part to sulfur dioxide, water and the insoluble sulfur and in part to hydrogen sulfide and sulfur trioxide. This latter hydrogen sulfide is then oxidized by the sulfur dioxide, sulfur being formed.

In this method 70 gm. of sulfuric acid (Sp. gr. 1.84) is weighed out in a beaker which is then cooled with ice. Then a solution of 30 gm. of sodium thiosulfate in 50 cc. of distilled water is added drop by drop from a separatory funnel. In this way the acid is kept cold and a uniform particle size is obtained. The resulting sol possesses a milky-yellow color and a strong odor of sulfur dioxide. It is then diluted with 300 cc. of distilled water and heated on a water bath for 10 minutes. This results in a removal of the sulfur dioxide and a precipitation of some of the sulfur which is filtered out with glass wool. After twenty-four hours the heating on a water bath and the

subsequent filtration is repeated twice. After three or at most four such treatments one obtains a hydrosol that does not give any precipitate on heating or upon standing.

In addition to the colloidal solutions of sulfur there are today also pastes of colloidal sulfur which may be dispersed in water to form the colloid solution.

The sulfur hydrosol prepared by the reaction of sodium thiosulfate with sulfuric acid may be changed into a paste form by determining the exact amount of sodium carbonate required to neutralize the free acid present, neutralizing, and then collecting the precipitate of sulfur which forms, due to neutralization, on a hardened filter. The sodium sulfate must not be removed by dialysis since it acts as a stabilizer for the sulfur. It may however be replaced by a corresponding amount of sodium chloride. The sulfur precipitate is then made into a paste with about 10 per cent. of water.

In the method utilizing the reaction between sulfur dioxide and hydrogen sulfide, colloidal sulfur, water, and pentathionic acid is formed. A saturated solution of sulfur dioxide in ice cold water is prepared. Hydrogen sulfide from a Kipp generator is then passed in, taking care to insure an even flow of the gas as a too rapid flow will produce a precipitate of part of the sulfur. When the hydrogen sulfide is in slight excess the process is stopped and the solution filtered through glass wool. Several portions of this hydrosol are now treated with various amounts of 5 per cent. sodium chloride solution to determine the optimum point of precipitation. Sodium chloride is accordingly added and the liquid allowed to stand several hours, the clear supernatant liquid decanted and the sulfur collected on a hard filter by means of a Büchner funnel. The precipitate on the funnel is then washed with a 4, 3, 2, 1 and 0.5 per cent. sodium chloride solution in sequence. The moist precipitate is now collected and kept in its moist condition. When diluted four times with water or even more it forms hydrosols which are quite stable.

Different samples were found to vary somewhat in composition. A representative analysis gave:

Sulfur	26 %
Sodium chloride	2.2%
Water	71.8%

Pure sodium chloride must be used in the process, inasmuch as other salts, e. g., those of potassium and magnesium, precipitate the

sulfur irreversibly. This latter process gives the better result when colloidal sulfur in paste form is desired.

Examination of the Chalks under Ultra-Violet Light. W. E. Naylor and A. Surfleet. *Pharm. J. 136,* 261 (1936). Samples of prepared chalk which were believed to be precipitated chalk on the basis of macroscopic and microscopic appearance were examined under filtered ultra-violet light. Comparing them with the appearance of authentic samples of precipitated and prepared chalk examined in this manner, the suspected adulteration was confirmed. Precipitated chalk gave a "smoky" grayish violet fluorescence and prepared chalk a flesh or peach colored fluorescence.

It was also possible to determine the type of chalk used in preparing a compounded powder (MacLean's powder) on the basis of its fluoresence under ultra-violet light.

A New Medicine "Granulin" (Salicylic Acid Compound with Nicotine). S. I. Schaschin. *Dermatol. Wochschr. 102,* 388 (1936), through *Squibb Abstr. Bull. 9,* 685 (1936). "Granulin" is prepared by the extraction of Nicotiana rustica with a 2 per cent. solution of salicylic acid in 70 per cent. alcohol for 15 days so that the final ratio of the constituents is 25:2:100 respectively. The tincture after filtration is light brown in color and it possesses a strong, bactericidal action, particularly against staphylococcic infections. The solution is toxic but in ordinary usage no cases of poisoning have been found. It is applied three times daily on cotton pledgets for several minutes. It is recommended in the treatment of sycosis, furunculosis, pyodermatitis, impetigo staphylogenes, etc. Ten cases of dermatoses of 18 days' to 5 years' duration were cured in 2-19 days with this material.

Microscopical Detection of Aleurone Granules in Flour by Staining. B. Broda. *Z. Unters. Lebensm. 70,* 470 (1935), through *Brit. Chem. Abstr.* B. *55,* 344 (1936). On account of the Mg. content, the globoids of the aleurone layer are stained by quinalizarin, Titan-yellow or azo-blue in alkaline solution, and they can be recognized with ease under the microscope. Of the cereals, maize and rice contain the fewest globoids. In barley they are very numerous and are characteristically arranged in several layers. Cereal flour is readily distinguished from potato, sago, banana, maranta, and tapioca flours by this means.

NEWS ITEMS

Professor Gathercoal Chosen as Remington Medal Recipient. The New York branch of the American Pharmaceutical Association recently announced Edmond Norris Gathercoal, Professor of Pharmacognosy at the School of Pharmacy of the University of Illinois, as the 1936 Remington Medalist. This annual award, to the man or woman who is designated by the donors as having done the most for American pharmacy during the preceding year, or whose efforts during a number of years have culminated during the year in results considered most important and advantageous to the profession, has been won by the Illinois teacher through his unceasing and untiring work as Chairman of the Revision Committee of the National Formulary VI. He has received a number of other recognitions, latest of which was the honorary degree of Master in Pharmacy from the Philadelphia College of Pharmacy and Science in 1934.

Buffalo College Dean Retires. From April 22 to 24 the University of Buffalo School of Pharmacy celebrated its fiftieth birthday, and, at the same time, observed the completion of fifty years of service by its Dean, Willis G. Gregory. The Dean's retirement, effective July 1, was announced, together with the appointment of his successor, Dr. A. B. Lemon, who has been a member of the Faculty since 1916.

Philadelphia College Sponsors Two Exhibits. On April 17 and 18 the general public of Philadelphia and vicinity had its third opportunity in as many years to see a scientific institution in actual operation. The occasion was the Science Day Exhibit at the Philadelphia College of Pharmacy and Science. All of the college's laboratories were open for inspection and the faculty and a chosen group of students were on hand to demonstrate the various pieces of equipment and apparatus used in every day classroom instruction and in the numerous research projects under way.

From May 9 to 16 the Gross Research Laboratory of the College occupied a large booth in the medical section of the second annual "Philadelphia on Parade" exhibition in that city's Commercial Museum. The display, which attracted widespread attention and much favorable comment, explained in detail the story of the chemistry of digestion and excretion as carried out in the regular processes of the organs of the human body.

A CORRECTION

In the April issue of the JOURNAL, page 157, there appeared a table of the chemical elements and their discoverers, in which there is an error, according to a reputable reader.

His letter, in part, follows—"There is an unfortunate error in this list, in that Dr. Yntema, one of the co-discoverers of Illinium, is listed as a Hindu. Dr. Yntema comes from the Dutch section of Michigan and his family has been in this country for at least three generations, having come originally from Holland. I knew him for a good many years when he was at the University of Illinois. He is now in the Department of Chemistry at the College of Medicine at St. Louis University."